Exosomal Y-RNAs as mediators of bioactivity of cardiac-derived cell therapy

Grant Award Details

Exosomal Y-RNAs as mediators of bioactivity of cardiac-derived cell therapy

Grant Type: Inception - Discovery Stage Research Projects

Grant Number: DISC1-08643

Project Objective: To explore the contribution of a class of small non-coding RNAs, the Y-RNAs, which are enriched in exosomes (exo) secreted from cardiosphere-derived cells (CDCs).

Investigator:

Name:	Linda Cambier
Institution:	Cedars-Sinai Medical Center
Type:	PI

Disease Focus: Heart Disease

Human Stem Cell Use: Adult Stem Cell

Award Value: $181,063

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Grant Application Details

Application Title: Exosomal Y-RNAs as mediators of bioactivity of cardiac-derived cell therapy

Public Abstract:

Research Objective

We propose to dissect the contribution of Y-RNAs, small non-coding RNA species enriched in CDC-exosomes, in mediating the effect of CDC-exosomes on cardioprotection and macrophage polarization.

Impact

Examining the contribution of highly represented RNA species in CDC-exo could allow a better understanding of the mechanism of action of CDC-exo and modulation of their cargo to enhance their potency.

Major Proposed Activities

- Epigenetic reprogramming.
  Effect of Y-RNA on the heritable changes in gene activity and expression that occur without alteration in DNA sequence, which could explain the sustained effects of CDC-exo.
- Cardioprotective role of Y-RNA is correlated with macrophage polarization.
  In vitro analyses of the anti-inflammatory pathway mediated by Y-RNA (IL10, anti-inflammatory cytokine, increase by Y-RNA).
- Structural analyses of Y-RNA fragment.
  Generation of mutated fragments resulting in a change in the secondary structure that could affect the function.
- Functional analyses of the Y-RNA/hnRNPH1 complex in crucial aspects of RNA processing (pre-mRNA splicing...) in normal and pathological conditions.

Statement of Benefit to California:

About 610,000 people, men and women, die each year from heart disease in the US (1 in every 4 deaths), motivating the development of more effective therapeutic strategies.

We propose to characterize the implication of Y-RNA, highly enriched in CDC-exosomes, in mediating cardioprotection following a heart attack. This characterization will allow a safe modulation of exosomal RNA content, opening up the possibility that exosomes may become next-generation off-the-shelf therapeutic products.

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